In contrast, oral rehydration therapy uses glucose to facilitate intestinal salt and water absorption, deficits being replaced over 6 to 12 hours. Sucrose has been substituted in some regimens because of its universal availability and diminished cost. Its efficacy approaches that of glucose despite dependency on intestinal disaccharidases for hydrolysis. Rice powder that contains glycine plus amylose and amylopectin (which can be hydrolyzed to glucose) will significantly lower stool output and duration of diarrhea when compared with the standard 2% glucose solutions. Homemade sugar-salt solutions are not recommended because of the risk of inappropriate reconstitution.

The WHO oral rehydrating solution contains sodium, 90 mEq per liter; potassium, 20 mEq per liter; chloride, 80 mEq per liter; bicarbonate, 30 mEq per liter, and glucose, 111 mmol per liter. The composition of this solution approximates conventional mixtures used to treat moderate dehydration intravenously except in its glucose concentration. The volume of fluid to be given orally or via nasogastric tube in the first six hours is derived from the estimated percent dehydration (50 to 100 ml per kg), maintenance needs (25 ml per kg per six hours) and projected ongoing losses (12 ml per kg per six hours). Two thirds of the total volume is replaced over four hours with the WHO oral rehydrating solution. The final third is given as free water over the next two hours to allow for renal excretion of excess solute. Alternatively, 100 ml per kg of the WHO solution may be given for four hours, followed by 50 ml per kg of water during the next two hours.

Subsequent oral therapy should provide for maintenance fluid and electrolyte requirements and for anticipated ongoing losses. Use of the WHO oral rehydrating solution during this maintenance phase is not recommended. A solution that contains about 30 to 50 mEq per liter sodium, 20 to 30 mEq per liter potassium and 2% glucose should be used for no more than 24 hours. Return to a non-lactose-containing formula should commence within 24 hours. Breast-feeding should be continued throughout the diarrhea.

Traditionally pediatricians have been warned against rapid rehydration, particularly in children with hypernatremia, to avoid seizures due to intracellular influx of water. Although oral rehydration therapy results in a more rapid fall in serum sodium levels when compared with intravenous therapy, the incidence of seizures is not increased. In one study, the risk of seizures was related to the initial serum sodium concentration rather than to the rate of fall in serum sodium concentration. In addition, the occasional hyponatremia measured after oral rehydration therapy seems to be clinically insignificant. In children with hypovolemic shock, this therapy should only be used after adequate volume expansion with intravenous fluids and when the child is alert enough to cooperate with the regimen. Vomiting is not a contraindication to oral rehydration therapy, as rapid restoration of volume seems to diminish vomiting. Failure can be anticipated if the loss exceeds 10 ml per kg per hour and in children with paralytic ileus, in those with known glucose or sucrose intolerance or when purge rates exceed 10 ml per kg per hour.

Despite these possible obstacles, oral rehydration therapy obviates the need for the intravenous administration of fluids in 75% to 95% of children treated for dehydration. Appropriate use and careful monitoring will assure the safety of oral rehydration, which represents a physiologic, noninvasive and potentially cost-effective alternative approach to the conventional management of diarrhea in childhood.

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Surfactant Treatment of the Respiratory Distress Syndrome

SOON AFTER the identification of dipalmitoylphosphatidylcholine as the principal compound in pulmonary surfactant and the recognition in 1959 that infants who died of the respiratory distress syndrome had abnormal surface properties of the lungs, aerosols of this compound were tried unsuccessfully as treatment for this disorder. In the 1970s, however, a sound scientific basis for treatment with natural surfactant was established in preterm animals. In 1980 the results of the first uncontrolled trial of the use of surfactant prepared from beef lung were published. Since then 15 studies have been published, of which 6 have been controlled, randomized clinical trials. While many of these have shown remarkable responses to surfactant, others have shown no effects, depending on the surfactant chosen for the studies.

Natural pulmonary surfactant is a complex mixture of phospholipids, neutral lipids and at least two classes of surfactant-specific proteins. Surfactant is present in the airways and alveoli as aggregates of various sizes, the most surface active being the largest. These large surfactant aggregates will rapidly absorb to and spread on an air-water interface to establish an equilibrium surface tension of about 25 dynes per cm. On dynamic compression of the surface film, surfactant will lower the surface tension to values less than 10 dynes per cm. These surface properties can be reproduced using carefully resuspended lipid extracts of natural surfactant that contain less than 1% protein. The technique of resuspension is critical to surface behavior, as the composition of a surfactant is less important than the aggregate form of the lipids in suspension. Further, synthetic lipid surfactants can have in vitro properties similar to natural surfactant, yet be inactive in vivo. A surfactant for clinical use is not a traditional single-component pharmaceutical; rather, surfactant is a mixture of compounds whose surface physical properties in vitro may not be sufficient for in vitro function. Responses to a surfactant may be predicted only from the effects on surfactant-deficient premature lungs.

Based on sound experiments in animals, two strategies for clinical trials have been used. In the initial pilot trial, ventilator-dependent infants with severe respiratory distress syndrome were treated with tracheal instillation of suspensions of surfactant in saline. In a number of subsequent trials, workers have tried to prevent the respiratory distress syndrome by treating at-risk infants with surfactant in the delivery room. Infants treated with synthetic surfactants have no immediate improvement in lung function. In contrast, infants treated with animal or human surfactants may have immediate im-

provement in lung function. Following injection of surfactant into the airways of infants with severe respiratory distress syndrome, a surfactant response is characterized by a rapid decrease in oxygen requirements. In some trials, the ventilatory support could be decreased as well. The response was better and more prolonged when treatment was given as soon as possible after initiating ventilation.

Infants treated in the delivery room have a lower incidence and severity of the respiratory distress syndrome than control infants. Overall, treatment at birth decreases the oxygen requirements and ventilator support variables of the treated infants relative to control infants. When the groups treated at birth or after the onset of the respiratory distress syndrome are combined, pneumothorax is decreased from 28% in control to 12% in treated infants, pulmonary interstitial emphysema is decreased from 38% in control to 6% in treated infants and bronchopulmonary dysplasia is decreased from 46% in control to 33% in the surviving treated infants. Mortality was 31% in control infants and 12% in treated infants. Thus, surfactant treatment lowered the incidences of the major pulmonary complications of the respiratory distress syndrome and mortality. Incidences of other nonpulmonary complications of prematurity such as intraventricular hemorrhage, necrotizing enterocolitis or severe retinopathy of prematurity either were unchanged or decreased numerically but not statistically.

Surfactant seems to be a major advance in the treatment of the respiratory distress syndrome. Surfactants tested to date have been "homemade" and are not licensed for clinical use. Standardized surfactant preparations are being evaluated in clinical trials for licensure by the Food and Drug Administration (FDA). At present, a physician can treat infants only by preparing a surfactant and obtaining the necessary FDA permission for experimental drug use.

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